Six Month, Open-Trial of Bupropion SR in Comparison to Methylphenidate in the Treatment of Adults with ADHD

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ABSTRACT

Objective: ADHD has become increasingly diagnosed and treated in adults. Treatment modalities have grown to include several antidepressants as well as stimulant medications. This study was designed to evaluate the effectiveness of bupropion SR compared to methylphenidate in an extended open-label study following a previously reported six-week, double-blind placebo-controlled trial of bupropion SR (1). Methods: Sixty subjects were selected using the Utah Criteria and DSM-IV for ADHD. Sixty percent were assigned to bupropion SR and 40% to placebo in a double-blind manner. Nonresponders to bupropion (n=22) were treated with methylphenidate in an open manner. Patients treated with placebo were treated with bupropion SR. Results: Response rate to bupropion SR in patients (n=38) treated in either the double-blind study or the open study was 43% as defined by a 40% improvement in the Wender Reimherr Adult Attention Deficit Disorder Scale (WRAADDS). In nonresponders subsequently treated with methylphenidate (n=16) the response measured in the same manner was 63% (p<ns). Conversely, in patients who continued in treatment for an extended 4-6 month time period, WRAADDS scores improved 65% over baseline with bupropion SR (n=10) and 59% with methylphenidate (n=8) Discussion: We found a lower frequency of response in adult ADHD with bupropion SR as opposed to methylphenidate. However, treatment with either medication produced equivalent levels of improvement at the 4 to 6 month evaluation in the subpopulation continuing on medication.

INTRODUCTION

Despite the increasing recognition of adult ADHD, there is a paucity of data on its treatment. Information on long-term outcome in adults is even more limited. Although the stimulants have been shown to be effective in adult ADHD, the multiple dosing, scheduled prescribing restrictions, anxiogenic properties, and abuse potential limit their usefulness in subgroups of adults. Despite the emergence of bupropion as a second-line agent for pediatric ADHD, data in ADHD adults are limited. There is a perception that stimulants produce a greater degree of improvement in the symptoms of ADHD than non-stimulants such as bupropion. We now report findings on an open-label, extended study of bupropion SR in comparison with methylphenidate.

METHODS

Design

- Following a randomized, double-blind, placebo-controlled, parallel group study (1), patients were allowed to participate in a 6-month open-label extension with treatment with either bupropion SR or methylphenidate.
- Bupropion SR responders were offered to continue on bupropion SR.
- Patients who received placebo in the 6 week study were offered bupropion SR.
- Patients who did not respond to bupropion SR in the 6 week study were offered methylphenidate.

Patients

- Adults underwent the SCID and had to meet both the Utah and DSM-IV criteria for ADHD.
- Excluded subjects with eating disorders, seizure disorders, bipolar, substance abuse disorders, situational stresses, pregnant or lactating women, subjects under custody of the criminal justice system and patients who might represent a risk of suicide.

Treatment

- Bupropion sustained release was initiated with 100 mg / day; titrated by 100 mg / day at weekly intervals to a target dose of 400 mg / day (200 mg twice daily). Methylphenidate was started at 10 mg T.I.D. and adjusted according to treatment response.
- Up to 24 weeks

Assessments

- Physician-rated Clinical Global Impression Scale (Global Severity and Improvement)
- Wender Reimherr Adult Attention Deficit Disorder Scale (WRAADDS)

  A 28-point clinician administered scale containing seven 4-point items; attention difficulties, hyperactivity/restlessness, temper, mood instability, over-reactivity, disorganization, and impulsivity.
- Weissman Social Adjustment Scale (WSAS)

  A clinician administered scale addressing overall social adjustment plus five specific components; work, social leisure, extended family, marriage, and parental functioning.

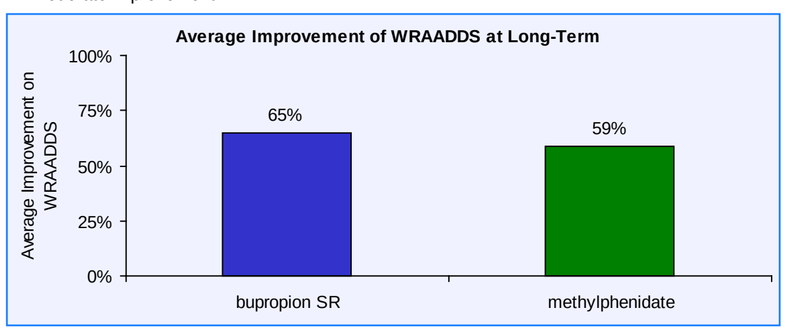
RESULTS

Demographics

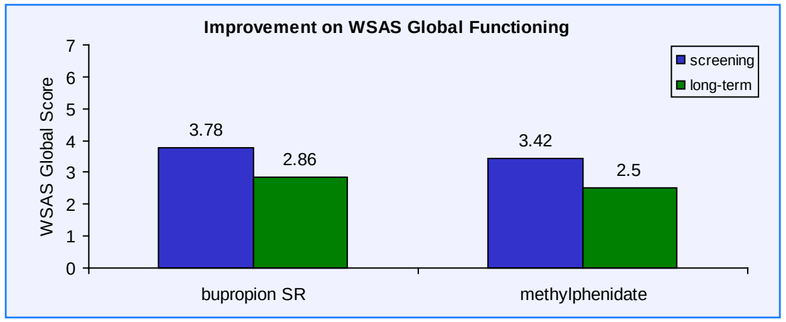
- 60 adults enrolled in the original double-blind study; 48 completed the double-blind study: 37 were enrolled in this extended open-label trial; 18 completed 16 or more weeks.
- 10 patients completed the open-trial on bupropion SR, 8 patients completed the open-trial on methylphenidate
- 6 women / 12 men
- Mean age ±SD: 34.6 ±11 years

Efficacy

- Average daily doses were 330 mg for bupropion SR and 37 mg for methylphenidate.
- Both bupropion and methylphenidate were well tolerated. No patients dropped out due to side effects.
- Both bupropion SR and methylphenidate were associated with a significant reduction in ADHD symptoms.
- At the long-term evaluation, bupropion SR was similar to methylphenidate in Clinical Global Improvement. Both groups had one patient with no change with the rest showing marked or moderate improvement.



- The 10 patients who completed 4 to 6 months treatment on bupropion SR showed a 65% improvement of WRAADDS scores.
- The 8 patients who completed 4 to 6 months treatment on methylphenidate showed a 59% improvement of WRAADDS scores.
- Individual components of the WRAADDS all replicated the overall changes.



- Bupropion SR and methylphenidate were both associated with an improvement in overall social adjustment.
- WSAS scores improved from an average between mild and moderate maladjustment to a average range between good functioning and mild maladjustment.
- Individual components of the WSAS all replicated the overall score.

CONCLUSIONS

- At the long-term evaluation improvement in ADHD symptoms was maintained in adults receiving bupropion SR or methylphenidate.
- Both bupropion SR and methylphenidate were well tolerated for up to 6 months.
- Limitations include small sample size, additionally, this study did not include a group of ADHD adults who failed methylphenidate who were then subsequently treated with bupropion SR.

REFERENCES

1. Reimherr FW, Hedges DW, Strong RE, Marchant BM, Williams ED, Wender P: 6-Week, Double-Blind, Placebo-Controlled Trial of Bupropion SR in the Treatment of Adults with Attention Deficit Hyperactivity Disorder (ADHD). Presentation at APA Conference, Chicago May 2000

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